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TITLE: Therapeutic multispecific compounds comprised of anti-Fc α receptor antibodiesSummary of Invention Paragraph (4):

[0004] IgA is abundant in the human body (Kerr, M. A. 1990, Biochem. J. 271:285-296). A single class of IgA Fc receptor, Fc α .RI or CD89, which binds to monomeric IgA has been identified and characterized (Albrechtsen, M. et al., 1988 Immunol. 64:201; Monteiro R., et al., 1990 J. Exp. Med., 171:597). Fc α .RI is constitutively expressed primarily on cytotoxic immune effector cells including monocytes, macrophages, neutrophils, and eosinophils (Morton, H. C., et al., 1996 Critical Reviews in Immunology 16:423). Fc α .RI expression on a sub-population of lymphocytes (Morton, H. C., et al., 1996 Critical Reviews in Immunology 16:423), and on glomerular mesangial cells has been reported (Gomez-Guerrero, C., et al., 1996 J. Immunol. 156:4369-4376). Its expression on monocytes and PMN can be enhanced by TNF- α . (Gesl, A., et al., 1994 Scad. J. Immunol. 39:151-156; Hostoffer, R. W., et al., 1994, The J. Infectious Diseases 170:82-87), IL-1, GM-CSF, LPS or phorbol esters (Shen L., et al., J. Immunol. 152:4080-4086; Schiller, C. A. et al., 1994, Immunology, 81:598-604), whereas IFN- γ . and TGF- β .1 decrease Fc α .RI expression (Reterink, T. J. F., et al., 1996, Clin. Exp. Immunol. 103:161-166). The α -chain of human Fc α .RI is a heavily glycosylated, type one transmembrane molecule belonging to the Ig super-gene family which also includes receptors for IgG and IgE. One gene located on chromosome 19 encodes several alternatively spliced isoforms of the Fc α .RI α chain (55-110 kDa; Morton, H. C., et al., 1996 Critical Reviews in Immunology 16:423). Myelocytic Fc α .RI has been shown to be associated with the Fc γ .-chain which is implicated as playing a role in Fc α .RI signal transduction (Morton, H. C. et al. 1995, J Biol. Chem. 270:29781; Pfefferkorn, L. C., et al. 1995, J. Immunol., 153:3228-3236, Saito, K. et al., 1995, J. Allergy Clin. Immunol. 96:1152).

Summary of Invention Paragraph (5):

[0005] Fc α .RI binds both antigen-complexed and monomeric IgA1 and IgA2 (Mazangera, R. L. et al., 1990 Biochem. J. 272:159-165), consistent with the receptor being saturated in vivo with monomeric IgA in the same manner as Fc γ .R and Fc ϵ .RI are saturated with IgG and IgE respectively. Cross-linking Fc α .RI on myeloid effector cells, by polymeric IgA, IgA immune complexes, or mAb specific for epitopes within or outside the ligand binding domain, stimulates degranulation, superoxide release, secretion of inflammatory cytokines, endocytosis and phagocytosis (Patty, C., A. Herbelin, A. Lihuen, J. F. Bach, and R. C. Monteiro. 1995 Immunology. 86:1-5; Stewart, W. W., R. L. Maz Yegera, L. Shen, and M. A. Kerr. 1994 J. Leukocyte Biology. 56:481-487; Stewart, W. W., and M. A. Kerr. 1990. Immunology. 71:328-334; Shen, L. 1992. J. Leukocyte Biology. 51:373-378.). These physiological responses triggered via Fc α .RI can be important in the first line of humoral defense on mucosal surfaces (Morton, H. C., M. van Egmond, and J. G. J. van de Winkel. 1996 Critical Reviews in Immunology. 16:423).

Detail Description Paragraph (50):

[0103] The multispecific molecules described above can be made by a number of methods. For example, both specificities can be encoded in the same vector and expressed and assembled in the same host cell. This method is particularly useful where the multi-specific molecule is a mAb.times.mAb, mAb.times.Fab, Fab.times.F(ab').sub.2 or ligand.times.Fab fusion protein. A bispecific molecule of the invention can also be a single chain bispecific molecule, such as a single chain

bispecific antibody, a single chain bispecific molecule comprising one single chain antibody and a binding determinant, or a single chain bispecific molecule comprising two binding determinants. Multispecific molecules can also be single chain molecules or may comprise at least two single chain molecules. Methods for preparing bi- or multivalent antibodies are described for example described in U.S. Pat. No. 5,260,203; U.S. Pat. No. 5,455,030; U.S. Pat. No. 4,881,175; U.S. Pat. No. 5,132,405; U.S. Pat. No. 5,091,513; U.S. Pat. No. 5,476,786; U.S. Pat. No. 5,013,653; U.S. Pat. No. 5,258,498; and U.S. Pat. No. 5,482,858.